REQUEST FOR RECONSIDERATION

Claims 1-5 and 7-12 are active in the case.

The rejection of Claims 3, 5 and 6 under 35 U.S.C. § 101 and 35 U.S.C. § 112 is traversed.

Claim 6 has been canceled. Claims 3 and 5 are not drafted as use claims, but merely further limit the medicine of Claim 3 and the medicinal composition of Claim 5 and, therefore, Claims 3 and 5 are directed to statutory subject matter.

The rejection of Claims 1-7 under 35 U.S.C. § 103(a) as being obvious over the combined teachings of Yazaki et al. I (WO 97/11068), II (US 5,998,436); and under the judicially created doctrine of obvious-type double patenting over Claims 1-11 of U.S. 5,998,436 and as directed to an invention not patentably distinct from Claims 1-11 of commonly assigned U.S. 5,998,436 is traversed.

Specifically, the compounds of the present invention, 1-(6-amino-3,5-difluoropyridin-2-yl)-8-bromo-7-(3-ethylaminoazetidin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (compound 1) and the maleate salt thereof (compound 2) are compared to compounds falling under the genus of compounds under Yazaki et al., but differing from the compounds of the present invention in that in comparative compound 1 (3-methylaminoazetidin-1-yl) is substituted for (3-ethylaminoazetidin-1-yl) in the compound of the present invention and in comparative compound 2 (8-chloro) is substituted for (8-bromo) in the compound of the present invention.

The antimicrobial effects, i.e., minimum growth inhibitory concentrations (MICs: μg/mL) were determined and the results are set forth on Table 1 on page 22 of the specification. The minimum inhibitory concentration (MIC) of compound 1 was approximately half of that needed for comparative compound 1 and comparative compound 2

to inhibit MRSE W200; one half to inhibit S.epidermidis IFO 12293 for compound 1 versus to comparative compound 1 and comparative compound 2; one half for E.faecalis IFO 12580 for compound 1 versus comparative compound 2; one half for M.luteus IFO 12708 for compound 1 versus comparative compound 2; one half for B.subtilis ATCC 6633 for compound 1 versus comparative compound 1; one half for P.vulgaris IFO 3167 for compound 1 versus comparative compound 2. Thus, compound 1 of the present claims exhibits superior antimicrobial effects, as compared to comparative compounds under the genus of Yazaki et al., against numerous microbes by indicating much lower minimum growth inhibitory concentrations are necessary.

A phototoxicity test was performed on mice and the results of the comparison between compound 1 of the present invention and comparative compound 1 and comparative compound 2, are shown in Table 2 on page 23 of the specification. Compound 1 of the present invention shows no ear abnormality and with none of three animals showing ear abnormality, while comparative compound 2 shows 0.7, or mild erythema, in 2 out of 3 animals at 0 hour. Therefore, compound 1 of the present invention shows superior or equal resistance to phototoxicity, as compared to a comparative compound under the genus of Yazaki et al.

Antibacterial effects on clinically-isolated quinolone resistant pneumococci were determined for compound 1 of the present invention against comparative compound 2, a compound under the genus of Yazaki et al. The results are shown in Table 3 on page 23 of the specification. Compound 1 of the present invention showed minimum growth inhibitory concentrations (MICs; μg/mL) of one half for compound 1 of the present invention against comparative compound 1 for isolated coccus 1 and less than one-fourth for compound 1 against comparative compound 1 for isolated coccus 5. Therefore, superior results are shown

for compound 1 of the present invention against a comparative compound under the genus of Yazaki et al. by showing much lower minimum growth inhibitory concentrations are necessary.

Finally, an *in vivo* pharmacokinetic study was made on the absorption and excretion of the compounds of the present invention and comparative compounds in and from dogs, specifically male beagles. The results are shown in Table 4 on page 25 of the specification. Compounds 1 and 2 of the present invention are compared to comparative compound 1 and the maleate salt of comparative compound 1, both compounds under the genus of Yazaki et al., with the maleate salt of comparative compound 1 being compared to compound 2, which is the maleate salt of compound 1 of the present invention. C_{max}(μg/mL) indicates a much higher concentration of the compounds of the present invention in the serum of the dogs after administration than that of the comparative compounds. The area under the serum concentration-time curve (AUC in μg.hr/mL) shows significantly higher values for the compounds of the present invention, as compared to the comparative compounds and the urinary excretion rate (%) is higher for the compounds of the present invention as compared to the comparative compounds. Thus, it can be seen that use of the compounds of the present invention results in much higher concentrations of the tested compounds in the serum within a comparable time period for the compounds of the present invention versus the comparative compounds with a significantly longer elimination half-life ($T_{\frac{1}{2}}$) for compound 1 versus comparative compound 1 and with a superior area under serum concentration-time curve (AUC) for the compounds of the present invention versus the comparative compounds and with an improved urinary excretion rate (%) for the compounds of the present invention as versus the comparative compounds. Therefore, the compounds of the present claims distinguish over Yazaki et al., because of the superior results shown above for compounds of

the present invention, as compared to compounds falling under the genus of Yazaki et al., but different from the compounds of the present invention.

The rejection of Claim 7 under 35 U.S.C. § 112, first paragraph is traversed.

The phrase "an infectious disease" has been deleted and the phrase "a microbial infection" has been substituted in its place. Antimicrobial effects have been shown throughout the present specification and examples. Further, Claim 7 has been amended to recite the phrase "an effective amount". Claim 7 meets the requirements of 35 U.S.C. § 112.

The rejection of Claims 1-5 under 35 U.S.C. § 112, second paragraph is traversed.

Claims 1-3 and Claims 2-5 are not substantial duplicates, since it is well settled in patent law that the Applicant may claim his invention in a number of different ways. Claim 1 is a compound claim. Claim 2 recites a medicine comprising as an active ingredient the compound of Claim 1 in an effective amount. Claim 3 recites the medicine as an antimicrobial medicine. Claim 4 claims a medicinal composition comprising an effective amount of the compound in a pharmaceutically acceptable carrier and Claim 5 recites the medicinal composition as an antimicrobial medicinal composition. The differing language in the claims clearly indicates that the claims are not substantial duplicates. Claims 1-5 meet the requirements of 35 U.S.C. § 112.

It is submitted that Claims 1-5 and 7-12 are allowable and such action is respectfully requested.

Respectfully submitted,

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MARKED-UP COPY OF AMENDMENT

IN THE CLAIMS

2. (Amended) A medicine comprising as an active ingredient an effective amount of 1-(6-amino-3,5-difluoropyridin-2-yl)-8-bromo-7-(3-ethylaminoazetidin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid or a salt thereof.

4. (Amended) A medicinal composition comprising an effective amount of 1-(6-amino-3,5-difluoropyridin-2-yl)-8-bromo-7-(3-ethylaminoazetidin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid or a salt thereof and a pharmaceutically acceptable carrier.

6. (Canceled).

7. (Amended) A method for the treatment of [an infectious disease] a microbial infection which comprises administering an effective amount of 1-(6-amino-3,5-difluoropyridin-2-yl)-8-bromo-7-(3-ethylaminoazetidin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid or a salt thereof.

8-12. (New).